

STIC Search Report Biotech-Chem Library

STIC Database Tracking Number: 125631

TO: David Venci

Location: 3d68

Art Unit: 1641

Friday, June 25, 2004

Case Serial Number: pctus0336133

From: Mary Hale

Location: Biotech/Chem Library

Rem 1D86 Phone: 2-2507

Mary.Hale@uspto.gov

Search Notes

David,

Here are the results from the lost, now found search. Two hits were retrieved.



Enter your Search Topic Information below:

PLEASE SEARCH CLAIMS 1 AND 2. FOR A DESCRIPTION OF "a-DICARBONYL COMPOUND," SEE SPECIFICATION P. 7, WHICH IS ATTACHED.

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Last Modified: 04/06/2004 12:14:41

and ADMA does not react with an α-dicarbonyl compound to form a

MA and arginine

of α-dicarbonyl compounds that are known in the art can be used in modify guanidino nitrogens of SDMA and arginine. The structure of a transformation compound is shown below.

Suitable a dicarbonyl compounds include, but are not limited to, dialdehydes, and diketones. Non-limiting examples of α-dicarbonyl compounds are biacetyl, pyrounic acid, glyoxal, methyglyoxal, deoxyosones, 3-deoxyosones, malondialdehyde, 2
(ΣΧΟΣΙΟΙΝΙΚ ΑΝΙΚΑΙ ΕΙΝΟΣΙΟΙΝΙΚΑΙ ΕΙΝΟΣΙΟΣΙΟΙΝΙΚΑΙ ΕΙΝΟΣΙΟΙΝΙΚΑΙ ΕΙΝΟΣΙΟΙΝΙΚΑΙ ΕΙΝΟΣΙΟΣΙΟΙΝΙΚΑΙ ΕΙΝΟΣΙΟΣΙΟΙΝΙΚΑΙ ΕΙΝΟΣΙΟΣΙΟΙΝΙΚΟΣΙΟΙΝΙΚΑΙ

[m many embodiments, R is a bulky group, including, but not limited to, a cyclopentyl group, a substituted cyclopentyl group; a six-membered ring, such as phenyl, a substituted phenyl (e.g., p-hydroxyphenylglyoxal, nitrophenylglyoxal, etc.), and the like. In embodiments of particular interest, the α-dicarbonyl compound is phenylglyoxal. The structure of phenylglyoxal is shown below.

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As one non-limiting example, where the α-dicarbonyl compoun reaction with arginine proceeds as follows:

The reaction with SDMA proceeds in a similar way.

In addition to reacting with the guanidino amine of arginine, phenylglyoxal has been reported to react with the α -amino group of the peptides to give α -keto acyl peptides. Takahashi (1968) *J. Biol. Chem.* 243:6171-6179. In the context of free amino acid, this observation indicates that phenylglyoxal will react with all α -amino groups of all amino acid.

=> fil reg COST IN U.S. DOLLARS

SINCE FILE SESSION ENTRY

FULL ESTIMATED COST

0.21 0.21

TOTAL

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STRUCTURE FILE UPDATES: 23 JUN 2004 HIGHEST RN 698346-19-9 DICTIONARY FILE UPDATES: 23 JUN 2004 HIGHEST RN 698346-19-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> e g E1 E2 E3 E4 E5	1 1	nitrogen/cn 5
=>		
=> e		
E6	1	GUANIDINOACETATE AMIDINOHYDROLASE/CN
E7	1	GUANIDINOACETATE KINASE/CN
E8	1	GUANIDINOACETATE METHYLTRANSFERASE/CN
E9	1	GUANIDINOACETATE METHYLTRANSFERASE (RAT STRAIN SPRAGUE-DAWLE Y)/CN
E10	. 1	GUANIDINOACETATE N-METHYLTRANSFERASE (HUMAN CLONE MGC:1854 I MAGE:2989341)/CN
E11	1	GUANIDINOACETATE N-METHYLTRANSFERASE (HUMAN CLONE MGC:24023 IMAGE:4246521)/CN
E12	1	GUANIDINOACETATE TRANSMETHYLASE/CN
E13	1 1	GUANIDINOACETIC ACID/CN
E14	1	GUANIDINOACETIC ACID Γ-LACTAM/CN
E15	1	GUANIDINOACETIC ACID HYDROCHLORIDE/CN
E16	1	GUANIDINOACETYL CHLORIDE HYDROCHLORIDE/CN
E17	1	GUANIDINOACETYLGLYCINE ETHYL ESTER HYDROCHLORIDE/CN
=> s guanidino(l)nitrogen?		

```
2013 GUANIDINO
         12936 NITROGEN?
L1
             O GUANIDINO(L)NITROGEN?
```

=> s quanidino?/cn

L2 34 GUANIDINO?/CN

```
=> s arginine/cn
L3
             2 ARGININE/CN
=> s "\alpha-dicarbonyl"/cns
       1621184 "A"/CNS
         41993 "DICARBONYL"/CNS
            15 "A-DICARBONYL"/CNS
L4
                  (("A"(W) "DICARBONYL")/CNS)
=> s (dialdehyde? or ketoaldehyde? or diketone? or biacetyl? or pyruvic acid or
glyoxal or methylglyoxal or deoxyosone? or malondialdehyde or oxopropanol or
phenylglyoxal or butanedione or cyclohexanedione)
           313 DIALDEHYDE?
             3 KETOALDEHYDE?
            49 DIKETONE?
            53 BIACETYL?
          1821 PYRUVIC
       6421742 ACID
          8525 ACIDS
       6428081 ACID
                  (ACID OR ACIDS)
          1754 PYRUVIC ACID
                 (PYRUVIC(W)ACID)
          2016 GLYOXAL
             1 GLYOXALS
          2016 GLYOXAL
                 (GLYOXAL OR GLYOXALS)
           103 METHYLGLYOXAL
             O DEOXYOSONE?
            42 MALONDIALDEHYDE
             3 OXOPROPANOL
           226 PHENYLGLYOXAL
         19804 BUTANEDIONE
         11846 CYCLOHEXANEDIONE
L5
         35678 (DIALDEHYDE? OR KETOALDEHYDE? OR DIKETONE? OR BIACETYL? OR PYRUV
               IC ACID OR GLYOXAL OR METHYLGLYOXAL OR DEOXYOSONE? OR MALONDIALD
               EHYDE OR OXOPROPANOL OR PHENYLGLYOXAL OR BUTANEDIONE OR CYCLOHEX
               ANEDIONE)
=> s (dialdehyde? or ketoaldehyde? or diketone? or biacetyl? or pyruvic acid or
qlyoxal or methylqlyoxal or deoxyosone? or malondialdehyde or oxopropanol or
phenylglyoxal or butanedione or cyclohexanedione)/cn
            22 DIALDEHYDE?/CN
             O KETOALDEHYDE?/CN
             2 DIKETONE?/CN
            42 BIACETYL?/CN
             1 PYRUVIC ACID/CN
             1 GLYOXAL/CN
             1 METHYLGLYOXAL/CN
             0 DEOXYOSONE?/CN
             1 MALONDIALDEHYDE/CN
             0 OXOPROPANOL/CN
             1 PHENYLGLYOXAL/CN
             1 BUTANEDIONE/CN
             1 CYCLOHEXANEDIONE/CN
L6
            72 (DIALDEHYDE? OR KETOALDEHYDE? OR DIKETONE? OR BIACETYL? OR PYRUV
               IC ACID OR GLYOXAL OR METHYLGLYOXAL OR DEOXYOSONE? OR MALONDIALD
               EHYDE OR OXOPROPANOL OR PHENYLGLYOXAL OR BUTANEDIONE OR CYCLOHEX
               ANEDIONE)/CN
=> e sdma/cn 5
E1
                   SDM 79/CN
             1
```

E2 1 SDM 801/CN 3 --> SDMA/CN E3 E4 1 SDMA (REDUCING AGENT)/CN E5 1 SDMF (HUMAN FETAL HEART REDUCED)/CN => s e3;d 1 cbib abs 3 SDMA/CN 'CBIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY' 'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY' The following are valid formats: Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats (RN = CAS Registry Number) REG - RN - Index Name, MF, and structure - no RN SAM FIDE - All substance data, except sequence data - FIDE, but only 50 names SQIDE - IDE, plus sequence data SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used - Protein sequence data, includes RN SQD3 - Same as SQD, but 3-letter amino acid codes are used - Protein sequence name information, includes RN SQN CALC - Table of calculated properties EPROP - Table of experimental properties PROP EPROP and CALC Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are: ABS -- Abstract APPS -- Application and Priority Information BIB -- CA Accession Number, plus Bibliographic Data CAN -- CA Accession Number CBIB -- CA Accession Number, plus Bibliographic Data (compressed) IND -- Index Data IPC -- International Patent Classification PATS -- PI, SO STD -- BIB, IPC, and NCL IABS -- ABS, indented, with text labels IBIB -- BIB, indented, with text labels ISTD -- STD format, indented OBIB ----- AN, plus Bibliographic Data (original) OIBIB ----- OBIB, indented with text labels SBIB ----- BIB, no citations SIBIB ----- IBIB, no citations The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available. The MAX format is the same as ALL. The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

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=> d ide 1

L7 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN

RN 30344-00-4 REGISTRY

CN L-Ornithine, N5-[bis(methylamino)methylene]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Ornithine, N5-(N, N'-dimethylamidino)-, L- (8CI)

OTHER NAMES:

CN SDMA

CN Symmetric dimethylarginine

FS STEREOSEARCH

DR 100663-65-8

MF C8 H18 N4 O2

LC STN Files: ANABSTR, BEILSTEIN*, BIOSIS, CA, CANCERLIT, CAPLUS, EMBASE, MEDLINE, TOXCENTER, USPAT2, USPATFULL

(*File contains numerically searchable property data)

DT.CA CAplus document type: Conference; Journal; Patent

RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

$$NH_2$$
 HO_2C
 S
 $(CH_2)_3$
 N
 $NHMe$
 $NHMe$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

96 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

98 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fil medl, hcap, biosis, embase, jicst, wpids

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION

155.12

154.91

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 07:33:11 ON 25 JUN 2004

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(M1) is useful for diagnosing various disorders such as hypertension, hyperhomocysteinemia, hyperglycemia, hypercholesterolmia, insulin resistance, renal insufficiency, congestive heart failure, atherosclerosis, transplant arteriopathy, by determining the level of ADMA in a biological sample. (M1) is useful for determining the extent, severity, progression or stage of a disorder for which an elevated ADMA level is diagnostic, for monitoring progression, or efficacy of a treatment, of a disorder for which ADMA level is diagnostic.

ADVANTAGE - (M1) enables detection of ADMA in a sample.
Dwg.0/0

- L15 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
 2001190656. PubMed ID: 11129410. Asymmetric dimethylarginine, derangements of the endothelial nitric oxide synthase pathway, and cardiovascular diseases. Boger R H; Bode-Boger S M. (Institute of Clinical Pharmacology, Medical School, Hannover, Germany.. boeger.rainer@mh-hannover.de) . Seminars in thrombosis and hemostasis, (2000) 26 (5) 539-45. Ref: 54. Journal code: 0431155. ISSN: 0094-6176. Pub. country: United States. Language: English.
- Analogues of L-arginine that are chemically modified at the AB terminal guanidino nitrogen group, such as Nomega-monomethy-L-arginine (L-NMMA), have been used for nitric KC633 S3 oxide synthase inhibition. However, L-NMMA and other methylated Larginine analogues are also endogenously formed. Among these, asymmetric dimethylarginine (ADMA) and symmetric dimethylarginine (SDMA) have been shown to be the most abundant. Like L-NMMA, ADMA is an inhibitor of NO synthase, whereas SDMA is inactive. ADMA is synthesized by N-methyltransferases, a family of enzymes that methylate L-arginine residues within specific proteins. Free ADMA is released during proteolytic cleavage of methylated proteins; it can be detected in plasma and urine, but its intracellular concentrations appear to be much higher. ADMA is metabolized by the enzyme dimethylarginine dimethylaminohydrolase (DDAH), and inhibition of DDAH activity has been shown to lead to increased ADMA levels and endothelial dysfunction. Plasma levels of ADMA are elevated in endstage renal failure, in atherosclerosis and hypercholesterolemia, in hypertension, and in heart failure. Although the molecular cause for elevation of ADMA concentration in these diseases has not been fully elucidated, evidence is accumulating that ADMA is one cause of endothelial dysfunction in these diseases. Moreover, it may be a marker or even a risk factor for cardiovascular disease. Therefore, pharmacological modulation of ADMA concentration may be a novel therapeutic target in cardiovascular diseases.
- => s (dialdehyde? or ketoaldehyde? or diketone? or biacetyl? or pyruvic acid or glyoxal or methylglyoxal or deoxyosone? or malondialdehyde or oxopropanol or phenylglyoxal or butanedione or cyclohexanedione or 14 or 15 or dicarbonyl?)) UNMATCHED RIGHT PARENTHESIS 'CARBONYL?))'
 The number of right parentheses in a query must be equal to the number of left parentheses.
- => s (dialdehyde? or ketoaldehyde? or diketone? or biacetyl? or pyruvic acid or glyoxal or methylglyoxal or deoxyosone? or malondialdehyde or oxopropanol or phenylglyoxal or butanedione or cyclohexanedione or 14 or 15 or dicarbonyl?) TOO MANY TERMS FOR FILE CROSSOVER IN L5
 There are limits on the size of an answer set being crossed over from one file to another. Enter HELP CROSSOVER at an arrow prompt (=>) for specific information.
- => s (dialdehyde? or ketoaldehyde? or diketone? or biacetyl? or pyruvic acid or glyoxal or methylglyoxal or deoxyosone? or malondialdehyde or oxopropanol or phenylglyoxal or butanedione or cyclohexanedione or 14 or dicarbonyl or 16)

```
L16
         20245 FILE MEDLINE
L17
        112591 FILE HCAPLUS
L18
         21049 FILE BIOSIS
L19
         23002 FILE EMBASE
         11554 FILE JICST-EPLUS
L20
L21
         10618 FILE WPIDS
TOTAL FOR ALL FILES
        199059 (DIALDEHYDE? OR KETOALDEHYDE? OR DIKETONE? OR BIACETYL? OR PYRUV
L22
               IC ACID OR GLYOXAL OR METHYLGLYOXAL OR DEOXYOSONE? OR MALONDIALD
               EHYDE OR OXOPROPANOL OR PHENYLGLYOXAL OR BUTANEDIONE OR CYCLOHEX
               ANEDIONE OR L4 OR DICARBONYL OR L6)
=> s (sdma or symmetric dimethylarginine or 30344-00-4 or 12 or quanidin? or 13 or
arginine?) and 122
L23
          1400 FILE MEDLINE
L24
          2935 FILE HCAPLUS
L25
          1226 FILE BIOSIS
L26
           913 FILE EMBASE
L27
            71 FILE JICST-EPLUS
L28
           162 FILE WPIDS
TOTAL FOR ALL FILES
          6707 (SDMA OR SYMMETRIC DIMETHYLARGININE OR 30344-00-4 OR L2 OR GUANI
               DIN? OR L3 OR ARGININE?) AND L22
=> s (sdma or symmetric dimethylarginine or 30344-00-4 or 12 or quanidin?) and (13
or arginine?) and 122
L30 ·
            65 FILE MEDLINE
L31
           187 FILE HCAPLUS
L32
            60 FILE BIOSIS
L33
            44 FILE EMBASE
L34
             1 FILE JICST-EPLUS
L35
             9 FILE WPIDS
TOTAL FOR ALL FILES
           366 (SDMA OR SYMMETRIC DIMETHYLARGININE OR 30344-00-4 OR L2 OR GUANI
               DIN?) AND (L3 OR ARGININE?) AND L22
=> s 136 and modif?
L37
            31 FILE MEDLINE
L38
            88 FILE HCAPLUS
L39
            38 FILE BIOSIS
L40
            24 FILE EMBASE
L41
             O FILE JICST-EPLUS
L42
             1 FILE WPIDS
TOTAL FOR ALL FILES
L43
           182 L36 AND MODIF?
=> s (sdma or symmetric dimethylarginine or 30344-00-4) and (12 or quanidin?) and
(13 or arginine?) and nitrogen and 122
L44
             O FILE MEDLINE
L45
             O FILE HCAPLUS
L46
             O FILE BIOSIS
L47
             O FILE EMBASE
L48
             O FILE JICST-EPLUS
L49
             1 FILE WPIDS
TOTAL FOR ALL FILES
L50
             1 (SDMA OR SYMMETRIC DIMETHYLARGININE OR 30344-00-4) AND (L2 OR
               GUANIDIN?) AND (L3 OR ARGININE?) AND NITROGEN AND L22
```

=> d

ANSWER 1 OF 1 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN L50 2004-431969 [40] WPIDS AN N2004-341454 DNC C2004-161888 DNN Detecting asymmetric dimethyl-arginine (ADMA) in sample having TΙ ADMA, symmetric dimethyl-arginine (SDMA) and arginine, for diagnosing hyperglycemia, by detecting ADMA after modifying SDMA and arginine using alphadicarbonyl compound. B04 D16 S03 DC IN COOKE, J; LIN, K Y (STRD) UNIV LELAND STANFORD JUNIOR PΑ CYC 107 PΙ WO 2004046314 A2 20040603 (200440)* EN 28 C12N000-00 RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW ADT WO 2004046314 A2 WO 2003-US36133 20031113 PRAI US 2002-426677P 20021115 ICM C12N000-00

=> log y

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 44.98 200.10

FULL ESTIMATED COST

STN INTERNATIONAL LOGOFF AT 07:40:07 ON 25 JUN 2004